Free Rad. Res. Comms., Vols. 12-13, pp. 675-680
Reprints available directly from the publisher
Photocopying permitted by license only

THE EVOLUTION OF OXIDATIVE STRESS INDICATORS IN THE COURSE OF MYOCARDIAL ISCHEMIA

J. LOEPER, J. GOY, JM KLEIN, M. DUFOUR, O. BEDU, S. LOEPER and J. EMERIT

Service de Médecine Interne du Professeur J. Emerit, Hôpital de La Salpétrière 47/83, bld de l'Hôpital 75013 Paris, France

Two studies were carried out in patients suffering from Unstable Angina (UA) and Myocardial Infarction (MI).

The first study investigated the variations of the Malondialdehyde (MDA) rate at 1st, 5th, 12th day of treatment in 27 patients (15 UA and 12 MI), compared to 15 controls.

This rate varied in a different way, with a first peak and a rapid decrease in UA, where it regularly decreases in MI.

The second study focused on the variations of MDA, Superoxide Dismutase (SOD), Glutathion Peroxydase (GPX) rates at 2nd, 12th days in 53 patients (19 UA and 34 MI), compared to 35 controls. Here again, the rate of MDA was high on day 2 and decreased on day 12. The rate of GPX showed similar evolution while the SOD rate had an opposite evolution.

These two studies confirm the evidence of oxidative stress in acute coronary deficiency.

KEY WORDS: Oxidative stress, myocardial infarction, unstable angina.

INTRODUCTION

It has now been demonstrated in animal studies, that Oxygen-Free Radicals (OFR) and lipid peroxidation play an important role in the course of ischemia-reperfusion.[1-3]

In man, this has not yet been demonstrated, and the purpose of this study is to find out whether the dosage of plasmatic Malondialdehyde (MDA) could vary in the course of acute coronary insufficiency, either in the case of Unstable Angina (UA) or Myocardial Infarction (MI).

A first study (S1) having demonstrated these variations, it was followed by a second one (S2), during which additional indicators of oxydative stress were measured in blood red cells, namely SOD and Glutathion peroxydase (GPX).[4]

MATERIALS AND METHODS

S1 concerns 27 patients compared to 15 controls;

S2 concerns 53 patients compared to 35 controls.

Controls were selected among nursing staff or consulting patients, and did not present any sign of coronary insufficiency.

Diagnosis

Patients were hospitalized for a painful, prolonged thoracic syndrome, typical of acute coronary insufficiency. The myocardial infarction in process was confirmed according to electrical (a characteristic electrocardiographical evolution, with appearance of necrosis Q-waves), and biological (increase of creatine phosphokinase rate and of CPK MB fraction, measured several times) criteria. The unstable angina was determined by an infarction threat syndrome with CPK rates remaining within normal values.

Dosage

MDA is a product of stable degradation, resulting from lipid peroxidation. It can be measured according to the Yagi technique, through the precipitation of plasma to phosphotungstic acid, and by measure of the fluorescence obtained with thiorbarbituric acid.[5,6] SOD is assessed by Crapo, McCord and Fridovich technique.[7] GPX is assessed by Paglia and Valentine technique.[8]

Method

S1 includes 15 UA and 12 MI, 19 men and 8 women, of average age 66 ± 13 years, with MDA dosage at D1, D5, D12; compared with 15 controls of average age 67 ± 13 years.

S2 includes 19 UA, 34 MI, compared with 35 controls, with MDA, and SOD and GPX intraglobular dosages at D2 and D12.

Results

The MDA rate varies according to a first increase, followed by a decrease in Unstable Angina, while it regulary decreases in Myocardial Infarction.

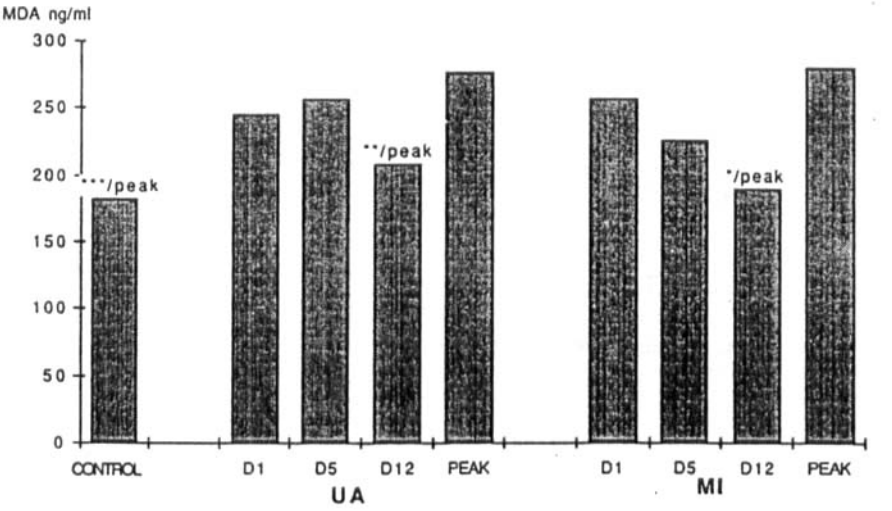

FIGURE 1 Plasmatic MDA in S1; *: $p < 0.05$; **: $p < 0.01$; ***: $p < 0.001$.

In S1 (Figures 1 and 5)

		MDA ng/ml
UA	D1	246 ± 64
	D5	257 ± 50
	D12	209 ± 35**/peak
	peak	277 ± 55
MI	D1	257 ± 83
	D5	226 ± 61
	D12	190 ± 44*/peak
	peak	281 ± 77
Control		183 ± 22***/peak

In S2 (Figures 2, 3 and 4)

		MDA ng/ml	SOD U/mg Hb	GPX U/g Hb
UA	D2	245 ± 75	5,08 ± 0,94	14,28 ± 4,79
	D12	233 ± 44	5,31 ± 1,40	12,23 ± 5,19
MI	D2	230 ± 76	5,11 ± 0,77	12,68 ± 5,9
	D12	206 ± 33*	6,06 ± 1,29*	10,70 ± 6,21*
Control		169 ± 12**	6,19 ± 1,29*	12,11 ± 6,00

* = $p < 0.05$
** = $p < 0.01$
*** = $p < 0.001$

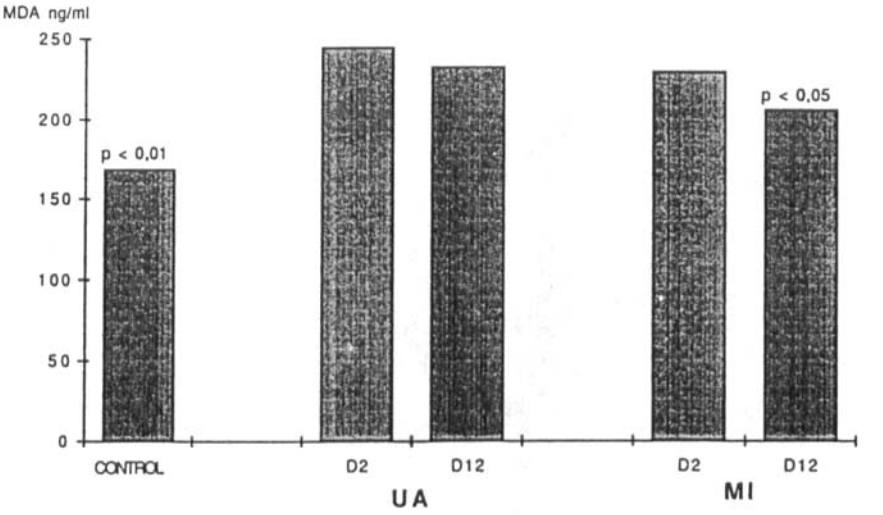

FIGURE 2 Plasmatic MDA in S2.

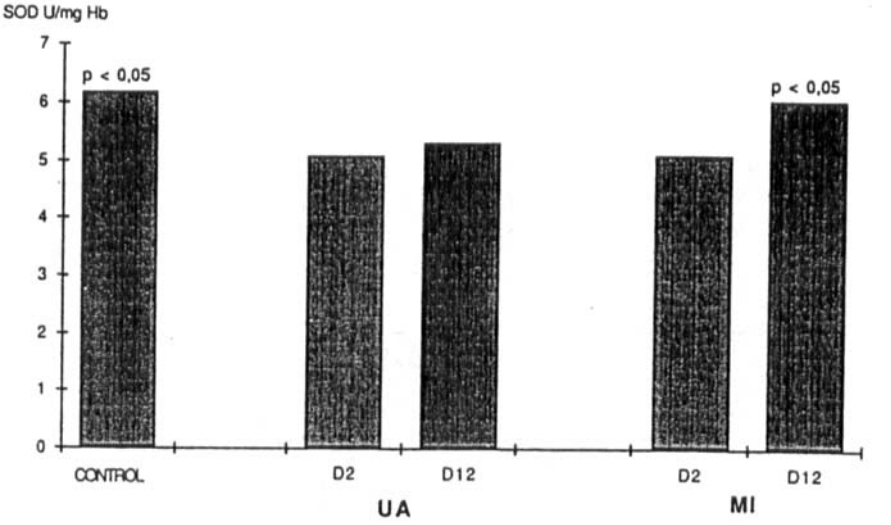

FIGURE 3 SOD in S2

These results show a significant increase of MDA in cases of acute coronary insufficiency ($p < 0.001$), whether they be MI or UA. Similarly, a significant decrase of intraglobular SOD in comparison with controls, may be noted.

MDA rates show an increase in the first two days of a MI or UA, in comparison with controls, with a subsequent decrease at D12.

SOD doses show a decrease at the beginning, returning to normal at D12, in cases of MI.

Variations of GPX rates are of minor importance and occur in the opposite way.

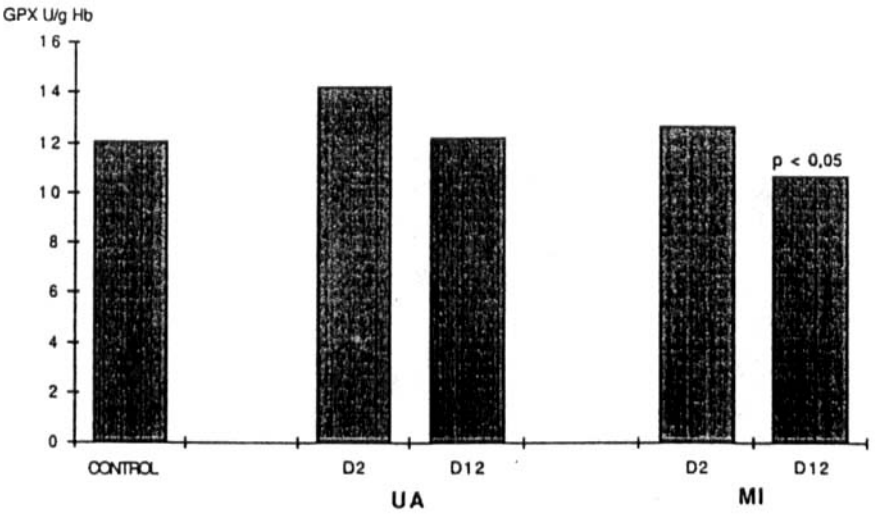

FIGURE 4 GPX in S2

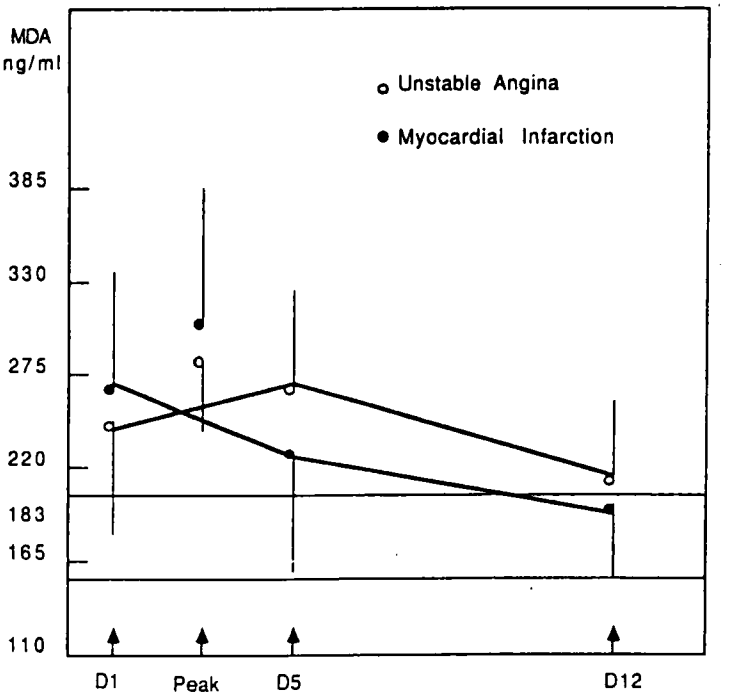

FIGURE 5 Plasmatic MDA in S1

DISCUSSION

The results of both studies show that the MDA rate is higher on the first two days of an acute coronary insufficiency, than on the 12th day. This proves the existence of lipid peroxidation in the course of acute coronary insufficiency, which tends to decrease within approximately ten days.[9-11]

This lipid peroxidation reflects in all likelihood an accumulation of polynuclear neutrophils and platelets, simultaneous with the obstruction of the coronary artery, its decrease within 12 days corresponding to the regression of this cellular infiltration in this time span.[12]

Peroxidation is in fact simultaneous with platelet aggregation (thromboxanes and leucotriens synthesis, enzymatic peroxidation by cyclo-oxygenase and lipoxygenase, as well as O2- secretion or non-enzyme peroxidation), and with polynuclear neutrophil activation.[10,12]

In this last case, O2- secretion is higher, but enzyme peroxidation can also be detected. Finally, endothelial cells are also capable of secreting O2-. Actually, it is difficult to determine which of the two types of peroxidation occurs, since these phenomena are intricate and these different cells are capable of exchanging ecosanoids between them.[12,13]

The first study shows a fact which corroborates this interpretation. Indeed, it is admitted that in a MI where MDA follows a progressively ascending curve from D1 to D5, the obstruction of the artery is considered complete. On the contrary, in UA,

the platelet clot disintegrates in the first days, and in our study, an MDA peak is observed at D5.[14]

However, MDA is a poor indicator of this lipid peroxidation, and the figures reported are only valid on a statistical basis and do not allow for follow-up of the evolution of one particular patient.

The second study shows, in parallel to lipid peroxidation and its regression, modifications at red blood cell level of GPX, which decreases, as well as an increase of SOD.

Therefore, oxydative stress in acute coronary insufficiency is reflected at the level of erythrocytes and decreases with time. These findings concur with the observations made in the course of alcoholic hepatitis.

References

1. J.M. McCord and I. Fridovich (1978) The biology and pathology of Oxygen Radicals. *Annals of Internal Medicine*, **89**, 122–127.
2. J.M. McCord (1988) Free radicals and myocardial ischemia: overview and outlook. *Free Radical Biology and Medicine*, **4**, 9–14.
3. K.P. Burton (1988). Evidence of direct toxic effects of free radicals on the myocardium. *Free Radical Biology and Medicine*, **4**, 15–24.
4. J. Fechner, J. Goy, J.Y. Artigou, O. Bedu, J. Loeper, J. Emerit Y. Grosgogeat (1986). Etude de la peroxidation lipidique membranaire au cours de l'insuffisance coronaire. *Press. Med.*, **15**, 1077–1080.
5. K. Yagi (1980). Toxicity of lipid peroxides in processed foods. *Biochemical Review*, **4**, 42–46.
6. K. Yagi (1982) Assay for serum lipid peroxide and its clinical significance. *Lipids peroxides in biology and medicine*. Academic Press, 223–242.
7. J.D. Crapo, J.M. McCord and I. Fridovich (1978). Preparation and assay of superoxide dismutases. *Method in Enzymology*. Vol. LIII, 382–393.
8. D.E. Paglia and W.N. Valentine (1967). Studies on the quantitive and qualitative characterization of erythrocyte glutathione peroxidase. *Journalot Laboratory and Clinical Medicine*, **70**, 1, 158–169.
9. M.L. Hess, M. Kontos and D.J. Hearse (1989). The role of oxygen-derived free radicals in the pathogenesis of myocardial ischemia and reperfusion- induced injury. In *CRC Handbook of Free Radicals and Antioxydants in Biomedicine*. J. Miquel, A.T. Quintanilha, H. Weber CRC Press, Boca Raton, Florida, pp. 275–285.
10. J. Emerit and J. Chaudiere (1989). Free radicals and lipid peroxidation in cell pathology. In *CRC Handbook of free radicals and antioxydants in biomedicine*. J. Miquel, A.T. Quintanilha, H. Weber, CRC Press, Boca Raton, Florida, pp. 177–185.
11. J.C. Dousset, M. Trouilh and M.J. Foglietti (1983). Plasma malonaldehyde levels during myocardial infarction. *Clinical Chimica Acta*, **129**, 319–322.
12. S.W. Werns, B.R. Lucchesi (1988). Leukocytes, oxygen radicals and myocardial injury due to ischemia and reperfusion. *Free Radical Biology and Medicine*, **4**, 31–37.
13. J. Loeper, J. Emerit, J. Goy, O. Bedu and J. Loeper (1983). Lipid peroxidation during human atherosclerosis. *IRCS Med Sci.*, **11**, 1034–1035.
14. S.W. Davies, K. Randjadayalan, D.G. Wickens, T.L. Dormandy, A.D. Timmis (1989). *European Heart Journal* **10**, *Abstr. Suppl.*, P 1409, 274.

Accepted by Prof. G. Czapski